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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,564	10/15/2004	Rajendra K Joshi	08201.0064-00000	4636

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EXAMINER	
VALENROD, YEVGENY	

ART UNIT	PAPER NUMBER
1621	

MAIL DATE	DELIVERY MODE
10/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,564	JOSHI ET AL.	
	Examiner	Art Unit	
	Yevgeny Valenrod	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,7-15 and 20-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,7-15 and 20-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/06/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Rejection under 35 USC 102 made over Schmidt et al. is withdrawn in view of applicants' amendment.

Rejection under 35 USC 102 made over Griffin is withdrawn in view of applicants' amendment.

Rejection under 35 USC 102 made over Stein et al is withdrawn in view of applicants' amendment.

Rejection under 35 USC 103 over Schmidt et al. is withdrawn in view of applicant' amendment.

Applicants' amendment to claims 18, 19 and 26 has overcome the rejections under 35 USC 101 and 35 USC 112.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 5, 7-15, 20-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 5 has been amended to

include a proviso that finds no support in the specification. Specification is silent as to which definitions of "n" are excluded when specific substituents corresponding to the definition of "R_1" and "R_2" are present.

Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 27-29 are directed to a method of treating a very large breadth of diseases encompassed by the terms autoimmune disease, host-versus-graft rejection and mitochondrial diseases.

"The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546.

a) Determining if any particular claimed compound would treat any particular autoimmune or mitochondrial disease would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of

fundamentally different diseases, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation.

b) The direction concerning treating autoimmune or mitochondrial diseases is found in the specification on page 10, which merely states Applicants' intention to do so. Applicants describe formulations in Examples 1-4. Doses required to practice their invention are not described in the specification. Since no compound according to claim 5 has ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these different diseases? Are the identical doses to be used for treating these unrelated diseases?

c) There are no working examples of treatment of any disease in man or animals. There are also no examples showing the compounds of the instant invention to have an effect on any mechanism that is correlated with any disease.

d) The nature of the invention is clinical treatment of disease with a pharmaceutical preparation that comprises the compound of claim 5.

e) The state of the clinical arts in treatment of mitochondrial and autoimmune diseases varies depending on the disease. Although there are known treatments for some of the disease, for example: L-DOPA replacement therapy for Parkinson's disease and corticosteroids for Multiple sclerosis, others have no specific treatment, for example Hashimoto's thyroiditis.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. One with such experience is able to administer therapeutic agents to the patients in need of treatment resulting from such

administration. One can determine the dosage within the scope of recommended dosages and monitor the progress and efficacy of treatment.

g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), Nationwide Chemical Corporation, et al. v. Wright, et al., 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), Ex parte Sudilovsky 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) In re Wright 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

h) The scope of the claims involves numerous materially different diseases embraced by the terms autoimmune, mitochondrial and host-versus-graft reaction. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make

and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

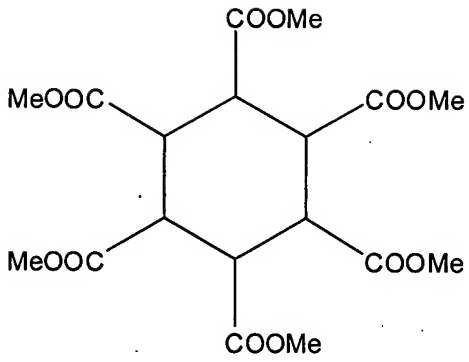
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

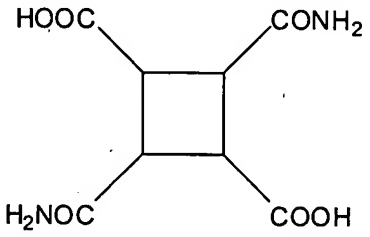
2. Claims 5, 7, 9, 13 and 14 rejected under 35 U.S.C. 102(b) as being anticipated by Kitchens et al. (US 5,042,986). Kitchens et al disclose trans-1, 2, 3, 4-cyclobutane tetracarboxylic acid.

3. Claims 5, 7, 9-12 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Farina et al. (*J. Am. Chem. Soc.* **1985**, *107*, 5100-5104). Farina et al disclose compound "1h" in the first column on page 5100. Compound 1h has the following structure:



The said compound anticipates the before mentioned claims when n = 3 and R_1 = R_2 = OMe.

4. Claims 5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Doerhoefer et al. (Tel. Let. 1966, 37, 4511-4516; see abstract and structure in the attached CAPLUS printout). A compound of the following structure is disclosed:



The said compound anticipates the before mentioned claims when: n = 2, R_1 = NH_2, and R_2 = OH.

Conclusion

Claims 5, 7-15 and 20-37 are pending.

Claims 5, 7-15 and 20-37 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yevgeny Valenrod whose telephone number is 571-272-9049. The examiner can normally be reached on 8:30am-5:00pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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